Neurology Asia 2017; 22(3) : 227 – 234

Clinical characteristics of chronic inflammatory demyelinatingpolyradiculoneuropathy in diabetes patients

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Abstract

Background & Objective: Co-exiting of CIDP and diabetes mellitus had been reported. Idiopathic CIDP(I-CIDP) is a treatable disease and had favorable response to immunosuppressive therapies but there is no established data for CIDP in diabetic patients (DM-CIDP). This study aims to determine clinical characteristics, phenotypes, electrophysiological tests and treatment response of CIDP in diabetic patients; and to determine the response to immunosuppressive therapy in DM-CIDP and I-CIDP.
Methods: The study was a retrospective chart review of Prasat Neurological Institute patients with diagnosis of CIDP between January 1st, 2008 and December 31th, 2015.
Results: Sixty four CIDP patients were identified, 12 were DM-CIDP and 52 were I-CIDP. Clinical characteristics, phenotypes, disease duration and disease severity in DM-CIPD were not different from I-CIDP. Demyelinating changes in nerve conduction studies were not different in the two entities but axonal features were more predominant in DM-CIDP. DM-CIDP also responded to immunosuppressive treatment, with modified Ranking Scale decreased after treatment as in I-CIDP. There was no difference in treatment response in DM-CIDP and I-CIDP.
Conclusion: Clinical characteristics, phenotypes, disease severity and treatment response to immunosuppressive treatment in DM-CIPD were not different from I-CIDP. Demyelinating features in nerve conduction studies were not different in the two entities but axonal features were more predominant in DM-CIDP.

Keywords: Chronic inflammatory demyelinating polyradiculoneuropathy, CIDP, diabetes mellitus, treatment response.

INTRODUCTION

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a symmetric, motor predominant, proximal and distal demyelinating peripheral neuropathy. CIDP is caused by an inflammatory or immune process against myelin proteins in peripheral nerves. The clinical course of CIDP is usually progressive for more than 8 weeks.[1,2] The reported prevalence and incidence of CIDP varied greatly in the medical literature. The reported prevalence of CIDP ranged from 1.9 to 7.7 per 100,000[3-6] and the incidence ranged from 0.15 to 0.48 per 100,000 person-years.[6-8]

Several variants of CIDP have been described based on the distribution of symptoms and signs.[9] In 2001, Saperstein *et al*.proposed that CIDP be classified as: 1) classic CIDP; 2) distal acquired demyelinating symmetrical neuropathy (DADS); 3) multifocal motor neuropathy(MMN) and 4) multifocal acquired demyelinating sensory and motor neuropathy (MADSAM).[10] CIDP is a treatable disease and many patients respond to immunosuppressive or immunomodulation therapies.[11-13]

CIDP has demyelinating feature in nerve conduction studies including: 1) Deceased motorconduction velocities; 2) Prolonged distal motor latencies; 3) Prolonged F-wave latencies; and 4) Temporal dispersion or conduction block.[9,14,15] Diabetic polyneuropathy (DPN) is a length-dependent, sensory predominant, axonal polyneuropathy caused by hyperglycemic state. Typically, DPN results in axonal degeneration and progressive loss of nerve fibers, as indicated by reduced compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) amplitudes, with normal or slightly

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decreased conduction velocities. However, demyelination changes in nerve conduction studies have been reported in DPN.[16,17] The co-existence of CIDP and DPN or CIDP in diabetes patients had been reported in the previous studies. Diabetes mellitus (DM) associated with CIDP was present in 9% to 26% of CIDP patients.[16-20]As the frequency of CIDP is higher in diabetic patients, it raise the question of whether these two disorders shared a common pathogenesis, or the association is just coincidental.

Identifying CIDP in diabetes patients is difficult because both entities, CIDP and DPN, can have similar clinical features including elevated CSF protein, and demyelinating features on nerve conduction studies. To date, there is no established criterion for the diagnosis of CIDP in diabetes patients.[18] However, recognition of CIDP in diabetic patient is important because CIDP is a treatable disease and many patients respond to immunosuppressive or immunomodulation therapies.[11-13] The excellent response to immunotherapy is already well established in CIDP patients without DM, but the evidence is less firm in CIDP patients with DM.[21]

The primary objective of the present study was to determine the clinical characteristics, clinical phenotypes, electrophysiological findings and cerebrospinal fluid findings of CIDP in diabetic patients in a single center. The secondary goal was to determine the response to immunosuppressive therapy for CIDP in diabetic and non-diabetic patients.

METHODS

After Institutional Review Board (IRB) approval, the disease diagnoses registries were searched for the potential diagnosis of CIDP or demyelinating neuropathy dating from January1st, 2008 to December 31th, 2015. CIDP patients were diagnosed using criteria proposed in 2010 by the European Federation of Neurological Societies/ Peripheral Nerve Society (EFNS/PNS guideline). This diagnostic criterion consists of clinical diagnostic criteria, electrodiagnostic criteria and supportive criteria.[12]

CIDP patients were categorized into definite, probable, and possible CIDP. All CIDP patients were included in the study. CIDP patients were classified as1) classic CIDP; 2) distal acquired demyelinating symmetrical neuropathy (DADS); 3) multifocal motor neuropathy (MMN) and 4) multifocalacquired demyelinating sensory and motor neuropathy (MADSAM).[9,10,12] The criteria for classification were: 1) Classic CIDP - chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities, developing over at least 2 months; cranial nerves may be affected; and absent or reduced tendon reflexes in all extremities. 2) DADS - Predominantly distal sensory neuropathy. When muscle weakness was observed, it was restricted primarily to distal muscle groups in a length-dependent fashion. 3) MADSAM - Asymmetric, multifocal acquired demyelinating sensory and motorneuropathy.

CIDP patient were classified into two groups; 1) CIDP in diabetic patients (DM-CIDP) and 2) CIDP in non-diabetic patients, idiopathic CIDP (I-CIDP). The diagnosis of diabetes was based on: 1) the presence of proved DM or 2) according to the American Association of Diabetes criteriabased on one of four abnormalities: hemoglobin A1C, fasting plasma glucose, random elevatedglucose with symptoms, or abnormal oral glucose tolerance test.[22]

To date, there is no established criterion for the diagnosis of CIDP in diabetes patients. CIDP with diabetic patients were included if patients had progressive symmetric, sensorimotor polyneuropathy with proximal predominant weakness or distal predominant weakness but had to have some degree of weakness in proximal muscles.Patients were excluded if 1) Patients were multifocal motor neuropathy (MMN) because treatment of MMN were different from CIDP. Prednisolone and plasma exchange are not effective in MMN and sometime associated with clinical worsening. 2) Patients had other causes of neuropathy such as from HIV, chronic kidney disease or hypothyroidism. 3) Diabetic patients who had atypical features from classic CIDP including asymmetric or pure sensory neuropathy.[18,20,23,24] Also excluded were patients with diabetic lumbosacral radiculoplexus neuropathy (DLSRPN) or other DPN.

Once the CIDP patients were identified, the medical records were reviewed to assess the demographic features, clinical manifestation, clinical phenotypes, disease duration prior to 1st evaluation, follow-up duration, clinical course, laboratory results including electrodiagnostic studies and CSF profiles, disease severity, disease disability, immunosuppressive treatment and treatment response to immunosuppressive treatment. Disease severity and disability were assessed and graded using modified Ranking Scale (mRS), mild disability with functional independence (mRS= 0–2), moderate disability

with functional partial dependence (mRS = 3) and severe disability with functional dependence (mRS = 4–5).

Disease remission means asymptomatic or stable disease activity in the patients who had been off treatment more than 1 year. Stable disease mean stable or improved disease activity in the patients who received immunosuppressive treatment more than 3 months and need to continue the treatment. Disease relapsing mean relapsed disease in patients who had been off treatment or remained on treatment.[25]

Statistical analysis

Descriptive summaries were presented as frequencies and percentages for categorical variables and median/mean and ranges for continuous variables. Comparisons between DM-CIDP versus I-CIDP were performed using Fisher's exact test or Wilcoxon rank sum test, as appropriate. All of the tests were two sided, and p-value less than 0.05 were considered asstatistical significance.

RESULTS

Demographic and clinical characteristics

Sixty four CIDP patients were included in the present study. Twelve were CIDP in diabetic patients (DM-CIDP) and 52 were CIDP in non-diabetic patients (I-CIDP). The demographic and clinical characteristics have been shown in

Table 1. The demographic and clinical characteristics of CIDP patients

	Total n = 64	DM-CIDP n = 12	I-CIDP n = 52	p-value
Sex (M:F)	1.1:1	1.4:1	1:1	0.603
Age at onset (years; median, IQ25,75)	48.7 (34.6, 61.8)	52.6 (49.1, 61.7)	46.2 (28.1, 61.8)	0.079
Age at evaluation (years; median, IQ25,75)	50.3 (34.3, 62.7)	53.4 (49.1, 62.1)	48.5 (28.2, 63.2)	0.118
Duration prior to 1st evaluation (months; median, IQ25,75)	5 (2, 8.8)	5 (2, 8)	4.7 (2, 9.5)	0.827
Less than 4 week (%)	15.6	8.3	17.3	0.668
Between 4 to 8 week (%)	11	16.7	9.6	
More than 8 week (%)	73.4	75	73.1	
Follow up duration (months; median, IQ25,75)	26.1 (6.8, 38.5)	19.8 (3.9, 44.9)	26.1 (9, 38.2)	0.613
Underlying disease				
No underlying disease (%)	79.7	0	98.1	1.000
Diabetes (%)	18.8	100	0	-
Others (%)	1.5	0	1.9	-
CIDP phenotypes				
Classic CIDP (%)	76.6	83.3	75	1.000
DADS (%)	18.8	16.7	19.2	-
MADSAM (%)	4.7	0	5.8	-
Clinical manifestation				
Sensorimotor (%)	84.3	100	80.8	0.490
Pure motor (%)	4.3	0	5.8	-
Pure sensory (%)	11.4	0	13.4	-
Autonomic symptoms (%)	0	0	0	NA
Respiratory failure (%)	1.6	0	1.9	1.000
Ophthalmoparesis (%)	4.7	0	5.8	1.000
Ptosis (%)	1.6	0	1.9	1.000
Bulbar involvement (%)	3.1	8.3	1.9	0.342
Symmetrical (%)	93.8	100	92.3	1.000
Hyporeflexia or areflexia (%)	93.8	100	92.3	1.000
Muscle atrophy (%)	14.3	16.7	13.7	1.000
Distribution of motor weakness				
Proximal greater or equal to distal (%)	62.5	75	59.6	0.508
Distal greater than proximal (%)	26.6	25	26.9	-
No motor weakness (%)	10.9	0	13.5	-
Sensory symptom				
Negative sensory symptom (%)	95.3	100	94.2	1.000
Pain (%)	14.1	16.7	13.5	0.672
Definite CIDP by EFNS/PNS criteria (%)	100	100	100	NA

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DM-CIDP in diabetic patients; I-CIDP, CIDP in non-diabetic patients; DADS, distal acquired demyelinating symmetrical neuropathy; MADSAM, multifocal acquired demyelinating sensory and motor neuropathy; EFNS/PNS, European Federation of Neurological Societies/Peripheral Nerve Society

Table 1. Age of disease onset of DM-CIDP patients was older than I-CIDP patients but the difference did not reach statistical significance (52.6vs. 46.2 years, p = 0.079). Of the 64 patients, 10 patients (15.6%) presented as acute onset CIDP mimicking AIDP with disease duration prior to diagnosis of less than 4 weeks. These patients received treatment as AIDP including intravenous immunoglobulin (IVIg) or plasmapheresis. There was no difference in term of disease duration prior to diagnosis, follow up duration, other underlying diseases, CIDP phenotypes and clinical characteristics of neuropathy in both study groups. The majority of DM-CIDP (83.3%) and I-CIDP (75%) presented with clinically classic CIDP. All the DM-CIDP patients and the majority of I-CIDP patients had symmetrical, sensorimotor, proximal and/ordistal weakness polyneuropathy with hyporeflexia or areflexia.

All the DM-CIDP patients had decreased sensation (100%) and pain was present in 16.7%. Bulbar involvement was uncommon (8.3%), and autonomic symptoms, respiratory failure, opthalmoparesis and ptosis were not seen in DM-CIDP as in I-CIDP.

Electrodiagnostic studies and CSF profiles

The electrodiagnostic studies and CSF profiles is shown in Table 2 and Table 3. All of DM-CIDP patients met definite EMG criteria. In I-CIDP patients, 96.2% met definite EMG criteria and 3.8% met possible EMG criteria. The frequency of electrodiagnostic abnormality were not different between both groups. However, the distal peroneal CMAP amplitude and the distal tibial CMAP amplitude of DM-CIDP were lower than I-CIDP, but did notreach statistical significance.

For CSF examinations,the median value of CSF protein in DM-CIDP was higher than I-CIDP (215 VS. 113 mg/dL, p=0.052).

Treatment outcome after immunosuppressive therapy

The study patients received variable regimens of treatment (Table 4). Most patients were treated with prednisolone or prednisolone and azathioprine. Other treatments were intravenous immunoglobulin, monthly intravenous pulse methylprednisolone, plasma exchange or combinations of the above mentioned. The treatment regimen, follow up duration, disease severity before treatment were not different between the two study groups.

The majority of DM-CIDP and I-CIDP patients had clinical improvement (mRS) after receiving the immunosuppressive treatment. The mRS after receiving immunosuppressive treatment were not different between DM-CIDP and I-CIDPpatients (p=0.373).

Table 2. Electrodiagnostic studies and CSF profiles of CIDP patients

	Total	DM-CIDP	I-CIDP	p-value
EMG criteria (EFNS/PNS criteria)	n = 64	n = 12	n = 52	
Definite (%)	96.9	100	96.2	1.000
Possible (%)	3.1	0	3.8	-
Nerve conduction study abnormality	n = 64	n = 12	n = 52	
Conduction block (%)	35.9	16.7	40.4	0.185
Slow conduction velocity (%)	79.7	75	80.8	0.697
Prolonged F-wave (%)	81.2	83.3	80.8	1.000
Prolonged distal latency (%)	76.6	83.3	75	0.715
Terminal latency index (TLI) less than 26 (%)	31.2	50	26.9	0.168
Cerebrospinal fluid examination	n = 61	n = 12	n = 49	
Protein (mg/dL; median, IQ25,75)	117 (79, 223)	215 (110, 263)	113 (63, 178)	0.052
Glucose (mg/dL; median, IQ25,75)	57 (57, 77)	80 (74, 89)	63 (55, 70.8)	0.000
Leukocyte (cell/μL; median, IQ25,75)	0 (0, 2)	0 (0, 2)	1 (0, 2)	0.385
Mononuclear cell (%; median, IQ25,75)	100 (100, 100)	100 (95, 100)	100 (100, 100)	0.158
Elevated CSF protein with leukocyte count less than 10 cell/μL (%)	86.9	91.7	85.7	1.000

CSF, cerebrospinal fluid; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DM-CIDP, CIDP in diabetic patients; I-CIDP, CIDP in non-diabetic patients; EFNS/PNS European Federation of Neurological Societies/ Peripheral Nerve Society

Table 3: Nerve conduction parameters of CIDP patients

	DM-CIDP	I-CIDP	p-value
Motor nerve study (median, IQ25,75)			
Right median nerve amplitude potential (mV)	3 (2, 5.6)	3.3 (1.6, 4.8)	0.923
Right median nerve conduction velocity (m/s)	31 (25, 42.6)	32 (23.8, 45.5)	0.879
Right median nerve distal latency (ms)	13.6 (6.1, 22.5)	9.3 (6.8, 12.2)	0.210
Left median nerve amplitude potential (mV)	3.2 (1, 4.5)	2.7 (1.4, 5.4)	0.569
Left median nerve conduction velocity (m/s)	39 (29, 50.6)	31 (25, 39)	0.101
Left median nerve distal latency (ms)	10.1 (5.5, 23.6)	9.9 (6.4, 13.3)	0.574
Right ulnar nerve amplitude potential (mV)	2.1 (1.2, 4.4)	3 (1.9, 5.3)	0.172
Right ulnar nerve conduction velocity (m/s)	32 (25, 44)	31 (23, 47.1)	0.971
Right ulnar nerve distal latency (ms)	5.9 (3.8,8.5)	6.3 (4.3, 8.1)	0.782
Left ulnar nerve amplitude potential (mV)	2.3 (1.1, 4)	2.8 (1.6 5.4)	0.241
Left ulnar nerve conduction velocity (m/s)	35 (26.6, 46.7)	34.1 (26.1, 45.9)	0.993
Left ulnar nerve distal latency (ms)	6.1 (4.6,12.2)	6.4 (4.5, 8.8)	0.637
Right tibial nerve amplitude potential (mV)	0 (0, 1.8)	1.1 (0, 3.4)	0.129
Right tibial nerve conduction velocity (m/s)	29.7 (23.5, 33.1)	28.7 (22.7, 38.3)	0.690
Right tibial nerve distal latency (ms)	10.1 (4.5, 20.3)	6.8 (4.9,10.9)	0.581
Left tibial nerve amplitude potential (mV)	0 (0, 1)	1.1 (0, 3.4)	0.073
Left tibial nerve conduction velocity (m/s)	33.3 (32.3, 35.8)	29 (23, 39.8)	0.524
Left Tibial nerve distal latency (ms)	10.8 (5.2, 23.4)	8.1(5.4, 12.4)	0.460
Right Peroneal nerve amplitude potential (mV)	0 (0, 0.6)	0.3 (0, 1.9)	0.097
Right Peroneal nerve conduction velocity (m/s)	36 (34.6, 45)	31.3 (22.1, 45)	0.407
Right peroneal nerve distal latency (ms)	14.2 (6.4, 20.1)	7.2 (5.6, 12.1)	0.336
Left peroneal nerve amplitude potential (mV)	0 (0, 0.6)	0.5 (0, 2.6)	0.073
Left peroneal nerve conduction velocity (m/s)	30 (25.1, 40.3)	37.9 (26, 43.1)	0.524
Left peroneal nerve distal latency (ms)	15.1 (6.5, 19.5)	8.6 (5.5, 10.5)	0.460
Sensory nerve study (median, IQ25,75)			
Right median nerve amplitude potential (μV)	0 (0, 0)	0 (0, 3.2)	0.195
Left median nerve amplitude potential (μV)	0 (0, 0)	0 (0, 0)	0.295
Right ulnar nerve amplitude potential (μV)	0 (0, 0)	0 (0, 8.6)	0.116
Left ulnar nerve amplitude potential (μV)	0 (0, 0)	0 (0, 10)	0.269
Right sural nerve amplitude potential (μV)	0 (0, 0)	0 (0, 0)	0.376
Left sural nerve amplitude potential (μV)	0 (0, 0)	0 (0, 0)	0.069
F-wave study (median, IQ25,75)			
Right median nerve F-wave (msec)	15 (0, 52.6)	0 (0, 34)	0.271
Left median nerve F-wave (msec)	31.7 (0, 54.8)	0 (0, 34.6)	0.097
Right ulnar nerve F-wave (msec)	15.7 (0, 45.3)	0 (0, 30.78)	0.227
Left ulnar nerve F-wave (msec)	31.3 (0, 43.7)	26.4 (0, 33.4)	0.262
Right peroneal nerve F-wave (msec)	0 (0, 0)	0 (0, 46.6)	0.118
Left peronealnerve F-wave (msec)	0 (0, 0)	0 (0, 32.5)	0.800
Right tibial nerve F-wave (msec)	0 (0, 44.2)	0 (0, 0)	0.713
Left tibial nerve F-wave (msec)	0 (0, 62.8)	0 (0, 49.2)	0.698

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DM-CIDP, CIDP in diabetic patients; I-CIDP, CIDP in non-diabetic patients; mV, millivolts; m/s, meter per second; ms, millisecond; μV, microvolt.

Table 4: Treatment and responsive to treatment of CIDP patients

	Total n = 64	DM-CIDP n = 12	I-CIDP n = 52	p-value
Treatment				
-Prednisolone (%)	31.2	25	32.7	0.318
-Prednisolone and Azathioprine (%)	17.2	33.3	13.5	
-Others[φ] (%)	51.6	41.7	53.8	
mRS at onset*				
Mild (0-2) (%)	14.1	8.3	15.4	0.605
Moderate (3) (%)	34.4	25	36.5	
Severe (4-6) (%)	51.6	66.7	48.1	
mRS at last follow up				
Mild (0-2) (%)	69.8	66.7	70.6	0.373
Moderate (3) (%)	22.3	16.6	23.5	
Severe (4-6) (%)	7.9	16.7	5.9	
Number of recurrent (median, IQ25,75)	0 (0,1)	0 (0,0)	0 (0,1)	0.172

*Other treatments included intravenous immunoglobulin (12.5%), monthly intravenous pulse methylprednisolone (9.4%), plasma exchange (1.6%), combinations of the previous mentioned (21.9%) and no treatment (6.2%).
CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DM-CIDP, CIDP in diabetic patients; I-CIDP, CIDP in non-diabetic patients; mRS, modified Ranking Scale.

Correlation between diabetes and treatment outcome

Subgroup analysis of 12 DM-CIDP patients showed that patients with mild neurological deficits (mRS 0-3) at last follow up had better diabetic control than patients with more severe neurological deficits (mRS 4-6) at last follow up (Fasting blood sugar at last follow up; 96 vs. 244 mg/dL; p-0.040). There was no difference in age, gender, duration of diabetes prior CIDP, mRS at onset, fasting blood sugar and HbA1C at diagnosis of CIDP among study groups (Table 5).

Table 5: Correlation between diabetes and treatment outcome inDM-CIDP patients

	Total n = 12	mRS at last follow up (0-3) n = 10	mRS at last follow up (4-6) n = 2	p-value
Sex (M:F)	1.4:1	1.5:1	1:1	1.000
Age at onset (years; median, IQ25,75)	52.7(48.5,61.7)	52.7(49.2,60.6)	63.1(48,78.2)	0.667
Duration of diabetes prior CIDP (months; median, IQ25,75)	72(0,120)	24(0,120)	120(120,120)	0.491
mRS at onset (points; median, IQ25,75)	4 (3,4)	4 (3,4)	4 (4,5)	0.165
FBS at diagnosis of CIDP (mg/dL; median, IQ25,75)	131 (107,161)	131 (102,182)	131 (122,139)	0.896
HbA1C at diagnosis of CIDP (mg%; median, IQ25,75)	7.2 (5.8,7.9)	7.4 (5.8, 8.2)	6.7 (6.7,6.7)	0.040
FBS at last follow up (mg/dL; median, IQ25,75)	100 (92,162)	96 (90,119)	244 (194,294)	0.617
HbA1C at last follow up (mg%; median, IQ25,75)	6.8 (6.3,7.5)	6.8 (6.3,7.5)	NA	NA

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; DM-CIDP, CIDP in diabetic patients; I-CIDP, CIDP in non-diabetic patients; mRS, modified Ranking Scale; FBS, fasting blood sugar; HbA1C, Glycosylated hemoglobin; NA, not available

DISCUSSION

This retrospective study demonstrated clinical and electrodiagnostic features of CIDP in Thai patients. Our results showed that the demographic, characteristics of polyneuropathy, electrodiagnostic features and CSF profiles were not different from previously described.[2,4,26]

DM-CIDP was common, 18.8% of CIDP patients in the present study had diabetes and were not different from previous studies, which showed 9% to 26%.[23] Diabetes is a common disorder, the chance of coexistence between CIDP and DM is possible but the hypothesis that diabetes is a risk factor for CIDP cannot be excluded. To-date, the explanation for the association between CIDP and DM is still unclear. However, it is importance to distinguishing CIDP from DPN in diabetes patients because CIDP is treatable disease. Immunotherapy in DM-CIDP patients may reduce neurological impairment, patient disability and quality of life. Under-diagnosis of CIDP indiabetic patients may thus lead to patient missing out on effective treatment.

In the present study, the demographic, clinical characteristics of CIDP, phenotypes, disease severity, disease duration prior to diagnosis and follow up duration were not different between DM-CIDP and I-CIDP. The majority of patients had clinically classic CIDP characterized by a symmetric, sensorimotor, proximal and distal weakness, hyporeflexia or areflexia, which progresses over 8 weeks. For electrodiagnostic investigation, all of DM-CIDP and I-CIDP patients met the criteria based on EFNS/PNS guideline in 2010. The frequency of abnormality in nerve conduction studies was not different between two study groups. However, the distal peroneal CMAP amplitude and the distal tibial CMAP amplitude in DM-CIDP patients were lower than I-CIDP patients. The demyelinating features in nerve conduction studies were not different between DM-CIDP and I-CIDP but DM-CIDP had more axonal changed in nerve conduction studies than I-CIDP patients. Even though there was evidence of axonal degeneration in DM-CIDP, but it was difficult to conclude that axonal degeneration in DM-CIDP was the consequence of axonal change from diabetic neuropathy. This was because of several I-CIDP patients also had lower CMAP amplitudes, from secondary axonal degeneration. Thus, the axonal degeneration in DM-CIDP could be a primary axonal change from diabetic neuropathy, as well as secondary axonal degeneration from demyelination.

In this study, the median CSF protein in DM-CIDP patients was 215 mg/dL (range 110, 263 mg/dL). Elevated CSF protein can be present in diabetic polyneuropathy but usually is not higher than 120 mg/dL. If the CSF protein is higher than 150 to 200 mg/dL, these are suspicion of super imposed inflammatory process.[20] The clinical of classic CIDP including symmetrical, sensorimotor, proximal and distal weakness, hyporeflexia or areflexia, which progresses over 8 weeks in combination with demyelinating changes in electrodiagnostic study and elevated CSF protein more than 120 mg/dL may be used to distinguish CIDP from DPN.[20]

In the present study, the responses to immunosuppressive treatment in DM-CIDP were similar to I-CIDP patients. Both DM-CIDP and I-CIDP patients had favorable response to immunosuppressive treatment. Majority of patients in both groups had some improvement, with the disabilities (mRS) better after immunosuppressive treatment. The disabilities of patients(mRS) before and after immunotherapy were not different between both study groups. This provide support to importance of identifying CIDP in diabetic patients. Our study showed that the DM-CIDP patients had favorable response to immunosuppressive treatment similar to I-CIDP patients. This might be related to rigid criteria for diagnosis of DM-CIDP as shown in the previous studies.[23,24] Only diabetes patients with clinical features of classic CIDP were included to the previous study. Clinically classic CIDP are progressive symmetric, sensorimotor polyneuropathy with proximal predominant weakness, or distal predominant weakness but with some weakness also in proximal muscles. Diabetic patients will be excluded from the study if the patients had one of the following features including: asymmetrical weakness, acute proximal leg pain followed by weakness as the pain settled. Fulfilling clinical and electrodiagnostic criteria of CIDP will excluded various types of diabetic neuropathy including DPN which are not responsive to immunosuppressive treatment.

For the effect of diabetes control and outcome of CIDP after treatment, the present study showed that patients with mild neurological deficits (mRS 0-3) at last follow up had better diabetic control than patients with more severe neurological deficits (mRS 4-6). The poorer response to treatment or more severe neurological deficit might be the result of diabetes neuropathy combine with demyelinating polyneuropathy. However, these results should be interpreted with caution

because of the small number of diabetic patients in the present study. Studies with larger number of patients are required to confirm our finding.

In summary, 1) the demographic, clinical characteristics, phenotypes, disease duration prior diagnosis, disease severity and response to immunosuppressive treatment of DM-CIDP patients were not different from I-CIDP patients. 2) DM-CIDP patients had demyelinating and axonal features in nerve conduction studies, which may be due to dual nerve pathologies from acquired demyelinating neuropathy and diabetic neuropathy. 3) Fulfilling electrodiagnostic criteria and clinical of classic CIDP, may help to identify CIDP in diabetic patients and 4) Recognizing DM-CIDP is important; under-diagnosis of CIDP in diabetic patients may lead to inadequate treatment of this group of patients.

DISCLOSURE

Financial support: None

Conflicts of interest: None

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